

Effectiveness of beta-blockers with neurocardiogenic syncope

Neurocardiogenic syncope and beta blocker

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Abstract

Aim: Syncope is a condition characterized by sudden and temporary loss of consciousness, accompanied by a loss of postural tone. In its pathophysiology, there can be a sudden drop in cerebral blood flow, alterations in the composition of the blood reaching the brain, or psychological causes. The aim of this study is to search the etiologies of syncope in children and evaluate the effectiveness of β -blocker treatment in cases with neurocardiogenic syncope.

Material and Methods: The study included 51 patients admitted to our hospital with syncope complaints over a period of 18 months. Patients were evaluated by history, physical examination, laboratory tests, Electrocardiography (ECG), 24-hour holter monitoring, tilt test and EEG. Patients with a positive tilt test were divided into two subgroups. One group was given β -blocker treatment, and the other group was given only recommendations.

Results: The tilt test was positive in 23 (45,09%) of 51 patients presenting with syncope complaints. Metoprolol was administered to 11 (21,56%) of the patients. Metoprolol was used as a β -blocker for 6 months. Conservative treatment was administered to 12 (23.52%) of them. The group not given β -blockers was advised to take enough water and salt, not to stand for long periods of time, raise the head of the bed by 20°, and not to get up suddenly from the bed or from where they were sitting. When the syncope recurrence was questioned at the end of the 1-year follow-up after treatment or offers, no recurrence of syncope was observed in patients who received or did not receive treatment.

Discussion: The tilt test is the only noninvasive test used in the definitive diagnosis of neurocardiogenic syncope and should be performed in doubtful cases to clarify the diagnosis. In the treatment and follow-up of patients with vasovagal syncope, it should be taken into consideration that some precautions before drug therapy may be sufficient. These suggestions are not to stand for a long time, to ensure adequate water intake, not fasting, to raise the head of the bed 20 degrees, and not to get up suddenly from the bed or sitting position. There are no difference between the two groups in terms of recurrence of syncope. β -blocker treatment has no effect on the recurrence of neurocardiogenic syncope.

Keywords

Tilt Test, Syncope, Neurocardiogenic Syncope, Electrocardiogram

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Introduction

Syncope is a condition characterized by sudden and temporary loss of consciousness, accompanied by a loss of postural tone [1,2].

In its pathophysiology, there can be a sudden drop in cerebral blood flow, alterations in the composition of the blood reaching the brain, such as hypercatecholamine and hypersympathetic nerve function, excessive vasorelaxation or relatively low blood volume or psychological causes [4].

Syncope can occur due to non-cardiac or cardiac pathologies. Non-cardiac causes include neurocardiogenic syncope, reflex mechanisms, orthostatic hypotension, psychogenic factors, metabolic or neurological causes, migraine, anxiety, cerebrovascular diseases, certain medications, and hyperventilation [3]. Cardiac causes may involve arrhythmic and non-arrhythmic factors.

The most common cause of syncope is vasovagal, also known as neurocardiogenic syncope. It is associated with insufficient maintenance of circulatory system continuity or adequate vasomotor tone during conditions such as postural changes, physiological alterations, volume loss, and emotional stress.

Lower extremity venous pooling leads to a decrease in venous return to the heart, resulting in a mild drop in blood pressure. Sympathetic activity increases, leading to enhanced ventricular contraction and a reduction in the left ventricular cavity. Ventricular mechanoreceptors are stimulated and transmitted to the brainstem via unmyelinated C fibers. In the efferent response of this reflex, sympathetic suppression occurs. This leads to vasodilation, slowing of heart rate, and a decrease in blood pressure [7].

The tilt test is the only test that can be used in patients suspected of having neurocardiogenic syncope. Patients with a positive tilt test can exhibit three types of responses to the test. The patient should rest for approximately 15 minutes before the test. The tilt table should be capable of being raised up to 90 degrees and should have supports for the feet [14].

While the patient is lying in a supine position, heart rate and blood pressure are monitored at five-minute intervals. After 15 minutes, the table is tilted to either 60 or 80 degrees, and measurements of heart rate and blood pressure continue. The tilt test can also be provoked with medication. Medications such as nitroglycerin, adenosine, or nitroprusside, isoproterenol, edrophonium, and epinephrine can be used [9].

In the vasodepressor type, only blood pressure drops, in the mixed type, blood pressure and heart rate drop, and in the cardioinhibitory type, only heart rate drops [11,12].

Material and Methods

This study was conducted on 51 patients, aged between 8 and 17 years (mean age: 13.147 ± 2.39), who presented with complaints of syncope to our hospital (between August 2001 and February 2003) during 18 months. Of the patients, 15 (29.4%) were male and 36 (70.6%) were female. Six patients (11.8%) presented with presyncope symptoms, while 26 (51%) had experienced a single syncopal episode, 13 (25.5%) had experienced 2 episodes, and 6 (11.8%) had experienced 3 or more syncopal episodes.

Detailed medical history was obtained from all patients, and

physical examinations were performed. Complete blood count, blood glucose, blood calcium, and ion levels were evaluated for all patients. ECG was performed to investigate possible cardiac pathologies, and PR, QRS, QT, and corrected QT were calculated. All patients underwent echocardiography, 24-hour Holter monitoring, and EEG.

A simple tilt test was administered to all patients. The patient was kept in the tilted position for 30 minutes, completing the total test duration in 45 minutes. If syncope or presyncope occurred, the test was terminated and considered positive. Positive test results were defined as a 30% decrease in heart rate based on the recorded maximum heart rate, and a 20% decrease in blood pressure based on the detected highest blood pressure.

In the study, out of the 51 included patients, the tilt test was negative in 28 (54.91%), and positive in 23 (45.09%). Among the consecutively positive tilt test results, beta-blocker treatment was initiated in 11 (21.56%) patients. Metoprolol was used as the beta-blocker. The subsequent 12 (23.52%) patients with positive tilts test did not receive any medical treatment but were provided with recommendations. These recommendations included avoiding prolonged standing, ensuring adequate water intake, not fasting for extended periods, elevating the head of the bed by 20 degrees, and avoiding sudden transitions from lying down or sitting. Prior to initiating medical treatment, epileptiform discharges were observed in one of the monitored cases during EEG, treatment was adjusted, and the case was excluded from the study.

The patients were evaluated twice with a 6-month interval and followed up for one year to inquire whether they experienced syncope or presyncope during this period. The statistical analysis was conducted using the SPSS for Windows release 6.1 software package. Chi-square, Kruskal-Wallis, Mann-Whitney U, Bonferroni test, and one-way analysis of variance tests were employed. A p-value of <0.05 was considered statistically significant.

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Results

A total of 51 patients presenting with syncope complaints were initially included in the study. However, one patient was excluded due to the diagnosis of epilepsy, and another patient did not attend the study. Forty-nine patients were included in the study. The ages of the study group ranged from 8 to 17 years (mean age: 13.14 ± 2.39). Thirteen of the patients were male (27%), while 36 were female (73%). It was observed that the number of females was significantly higher than males ($p < 0.003$) (Table 1).

In one case, Holter monitoring revealed ventricular premature beats at a rate of 12%. However, since there were no syncope or presyncope attacks during these premature beats, they were classified as benign premature beats.

The number of syncopal episodes varied among the groups, with a maximum of 2 in the tilt test negative group, 5 in the tilt test positive group receiving treatment, and 3 in the untreated group. There was a significant difference in the number of syncopal/presyncopal episodes among the three groups

Table 1. Age and Gender Distribution of Patients According to Tilt Test Results.

Tilt test result	Male		Female		Total		Age	Average ±SD	N	%
	n	%	n	%	n	%				
Tilt (-)	8	28,6	20	71,4	28	57,1	8.17	12,5 ±2,2	28	57,1
Tilt (+), treatment (+)	3	30	7	70	10	20,4	11,17	13,8 ±2,1	10	20,4
Tilt (+), treatment (-)	2	18,2	9	81,8	11	22,5	8.17	14 ±2,7	11	22,5
Total	13	27	36	73	49	100	8.17	13,2 ±2,4	49	100

Table 2. Number of syncope episodes at presentation.

Recurrence of syncope	Tilt (-)		Tilt (+)treatment (+)		Tilt (+)treatment (-)		Total	
	n	%	n	%	n	%	n	%
Presyncope	2	7,2	1	10	3	27,2	6	12,5
1 time	20	71,4	1	10	5	45,4	26	53
2 times	6	21,4	5	50	2	18,2	13	26,5
3 times			1	10	1	9,2	2	4
4 times			1	10			1	2
5 times			1	10			1	2
Total	28	100	10	100	11	100	49	100

Table 3. Comparison of 30th. minute systolic, 45th. minute systolic, and 45th. minute diastolic blood pressures between two groups.

Pairwise group comparison			p
	Tilt (-)	Tilt (+), treatment (+)	
30. minutes systolic BP	Tilt (-)	Tilt (+), treatment (+)	0,191
	Tilt (-)	Tilt (+), treatment (-)	0,06
	Tilt (+), treatment (+)	Tilt (+), treatment (-)	1
45. minutes systolic BP	Tilt (-)	Tilt (+), treatment (+)	0,001
	Tilt (-)	Tilt (+), treatment (-)	0,101
	Tilt (+), treatment (+)	Tilt (+), treatment (-)	0,442
45. minutes diastolic BP	Tilt (-)	Tilt (+), treatment (+)	0
	Tilt (-)	Tilt (+), treatment (-)	0
	Tilt (+), treatment (+)	Tilt (+), treatment (-)	0,38

(p=0.008) (Table 2).

All three groups were evaluated in terms of hemoglobin, sodium, potassium, calcium, creatinine, and blood sugar levels, heart rate, PR interval on the EKG, and QRS interval on the EKG, and no significant differences were found in any of these parameters.

Echocardiography results did not reveal any pathological findings that could be the cause of syncope.

EEG results were evaluated; in the group with a negative tilt test, cortical irritability in the frontal region was observed in 1 patient, and in the untreated group, epileptic discharges were detected in 1 case. These patients were excluded from the study.

All patients underwent tilt testing. The tilt test was positive in 23 cases (45,09%). In 2 of these patients, presyncope occurred during the test, and in 2 others, syncope occurred, leading to the termination of the test. A vasodepressor-type response was observed in 14 patients (60%), while mixed-type response was observed in 9 patients (40%). No cardioinhibitory-type response

was observed in any of the patients. When comparing the three groups, a significant difference was found in systolic blood pressure at 30 minutes, and systolic and diastolic blood pressure at 45 minutes between the group with negative tilt test and the groups with positive tilt test (p < 0.01) (Table 3). Beta-blocker treatment with metoprolol was administered to consecutive 11 (21,56%) patients with positive tilt tests for a period of 6 months. One patient was excluded from the follow-up due to non-compliance. The subsequent 12 (23,52%) patients with positive tilt tests did not receive treatment. In one of these patients, epileptiform discharges were observed in the EEG, and they were excluded from the study. The group without beta-blocker treatment was given advises.

At the end of the 1-year follow-up period after treatment or recommendations, when recurrence of syncope was queried, in the group with negative tilt tests, 2 patients experienced presyncope once, and 1 patient experienced syncope once. In both the treated and untreated groups, no recurrence of syncope was observed (p=0.596).

Discussion

Syncope is characterized by a sudden decrease in cerebral perfusion leading to a transient loss of consciousness accompanied by a loss of postural tone [1,2-12]. Up to 15 percent of children experience a syncopal episode prior to the end of adolescence [5].

This study provides valuable insights into determining the etiology of syncope in children and evaluating the effectiveness of β-blocker treatment in cases of neurocardiogenic syncope.

The most common cause of syncope is neurocardiogenic syncope [6]. The etiology of syncope was found to be related to neurocardiogenic and psychogenic factors in 40%, central nervous system in 32%, cardiac in 8%, medication and metabolic factors in 7%, and in 13% of cases, no specific cause was identified [6]. In our study, epilepsy was identified as the cause in 1.9% of cases presenting with syncope, and neurocardiogenic syncope was determined in 41.17%. In 56.93% of cases, no specific cause was found. However, no pathology was detected in repeated physical examinations and investigations, and these patients were referred to the pediatric health and child psychiatry outpatient clinic for further follow-up.

The tilt test is the only test that can be used in patients suspected of having neurocardiogenic syncope. Its use is still recommended for the diagnosis of TLOC by both the American College of Cardiology/American Heart Association/Heart Rhythm Society (ACC/AHA/HRS) and the European Society of Cardiology (ESC) guidelines [11,12].

ECG may be useful in explaining the etiology if the cause of syncope is cardiac in origin. In our study, all ECG results were found to be normal and did not provide useful information in explaining the etiology. In some studies conducted, it has been observed that echocardiography does not provide additional clinical benefit in patients with normal ECG and no history of cardiovascular disease [10].

The role of 24-hour Holter monitoring in diagnosing syncope is debated. This is because the patient may not experience symptoms or have a syncope episode during the 24-hour period in which the Holter device is attached.

EEG studies conducted on patients presenting with syncope have shown that only 1% of patients had epileptiform abnormalities. In our study, epilepsy was detected in 1 patient (1.9%), and treatment was arranged accordingly.

In a study conducted by Pongiglione et al., they found a vasodepressor response in 12.5%, mixed type in 68.5%, and cardioinhibitory response in 19% of cases [13]. In our study, vasodepressor response was observed in 12 patients (52.2%), while mixed type response was seen in 9 patients (47.8%). No patient exhibited a cardioinhibitory response.

In a study by Alehan et al., involving 20 cases suspected of neurocardiogenic syncope in patients aged between 12 ± 2.5 years, all patients were given β-blockers. At the end of an 18 ± 6 months follow-up period, no recurrence of symptoms was observed, and they stated that β-blocker use significantly reduced the recurrence of syncope [8].

In the present study, we gave β-blockers to 10 out of 21 cases suspected of neurocardiogenic syncope, and provided recommendations to the remaining 11 patients. After a 12-month follow-up, when we inquired about the recurrence of syncope or presyncope, we found that none of the patients experienced a recurrence of symptoms.

Conclusion

In our study, we found that the history of syncope was significantly more in girls compared to boys. This result was found to be statistically significant. Among the cases presenting with syncope, epilepsy was detected in 1.9%, while neurocardiogenic syncope was identified in 41.17%. In 56.93% of cases no specific cause could be determined.

None of the patients showed electrolyte imbalance as a cause of syncope. Similarly, none of the patients with syncope attacks were attributed to cardiac pathology.

Regarding the tilt test results, vasodepressor and mixed-type responses were observed in the patients, while cardioinhibitory type responses were not observed.

Eleven (21,56 %) patients with a positive tilt test were diagnosed with neurocardiogenic syncope and prescribed beta blockers, 12 (23.52%) patients were not given beta-blocker treatment and only recommendations were made. After a one-year follow-up period, none of the patients experienced a recurrence of syncope. This indicates that beta-blocker therapy may not be as crucial for neurocardiogenic syncope and that recommendations alone can be equally valuable as medication treatment. In every case of syncope, a detailed history should be taken and a careful physical examination should be performed. In all cases, a routine ECG should be obtained.

Further examinations are required in the differential diagnosis of syncope due to neurological or cardiological causes.

The tilt test is the only noninvasive test used in the definitive diagnosis of neurocardiogenic syncope and should be performed in doubtful cases to clarify the diagnosis.

In the treatment and follow-up of patients with vasovagal syncope, it should be taken into consideration that some precautions before drug therapy may be sufficient. These suggestions include not standing for a long time, ensuring adequate water intake, not fasting, raising the head of the bed 20 degrees, and not getting up suddenly from the bed or sitting position. We concluded that the use of β-blockers in the treatment of neurocardiogenic syncope is not more valuable than the recommendations.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and Human Rights Statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

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Conflict of Interest

The authors declare that there is no conflict of interest.

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